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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,980	04/03/2007	Roland Reiner	Q99617	7700

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EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
02/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,980	REINER ET AL.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The filing of a Preliminary Amendment on 10/30/2006, cancelling claims 1-22 and presenting new claims 23-48 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38 recites the terms, 'marker substances'. The specification (page 9, line 27) does not provide a definition for the said terms. In the absence of a definition any substance that is seen to fit the said terms will be considered as marker substance.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required

feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 41 recites the broad recitation complexing agent, and the claim also recites EDTA which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 23-25, 27, 38, 42-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Marler et al (Plast. Reconstr. Surg., 2000, 105, 2049-2058; document cited in International Search Report of 10/16/2006).

Marler et al teach tissue augmentation (increasing shape and volume) via subcutaneous injection of a composition comprising an alginate, into a rat (page 2049 Abstract, first, second and last paragraphs; page 2050, right column, first full paragraph; limitation of claim 23). The composition comprised of 1% medium viscosity alginate and a medium viscosity alginate covalently bonded to RGD-a cell adhesion peptide (limitations of claims 24, 25, 27, 38, 42). The alginates were used in cell culture medium to provide nutrients and phosphate buffered saline (page 2050, right col., last paragraph; limitations of claims 38, 43). The alginate was reconstituted as a 2% solution and gelled via crosslinking with calcium ions (page 2051, left col.,

first full paragraph). The alginate solutions with or without the cells were allowed to gel in vivo, after injection of a mixture of alginate, cell and calcium ions (page 2051, right column, first paragraph; limitations of claim 44).

Claims 23-25, 29, 31 and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Bent et al (Neurourology and Urodynamics, 2001, 20, 157-165; document cited in International Search Report of 10/16/2006).

Bent et al teach the treatment of incontinence by injection of alginate solution crosslinked (gelled) with calcium ions and containing chrondrocytes, into the sphincter muscle (page 157, abstract through page 158, middle).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24, 26, 28, 30, 32-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marler et al (Plast. Reconstr. Surg., 2000, 105, 2049-2058; document cited in International Search Report of 10/16/2006), in view of Bent et al (Neurourology and Urodynamics, 2001, 20, 157-165; document cited in International Search Report of 10/16/2006), Agerup (US 5,633,001; document cited in International Search Report of 10/16/2006), Vanderhoff et al (WO 96/39464; document cited in International Search Report of 10/16/2006), The Merck Index (12th Edition, 1996, page 758, entry # 4465) and Hawley's Chemical Dictionary (1997, page 1092).

This rejection is for claim limitations not covered by the anticipation rejection above.

The teachings of Marler and Bent are elaborated above. However, Marler et al and Bent et al do not teach the use of microparticles of alginate crosslinked with barium even though the use of alginate microparticles are disclosed, and injection into muscle tissue.

Agerup, drawn to method of tissue augmentation, teaches enlargement of tissue (same as increasing volume) like oesophagus, various sphincters, urether and rectum via injection of a composition comprising a carrier gel, which could be alginate (0.05-50%) in combination with tissue augmenting substance, which could be a carbohydrate polymer (col. 1, lines 5-16; col. 2,

lines 45-59). The composition can additionally contain therapeutically active substances like growth factors, hormones, vaccines, cytokines, antivirals, bactericidal compounds and other pharmacologically active compounds (col. 2, line 65 through col. 3, line 8). Example 2 teaches the use of alginate as a carrier gel, which is made harder (i.e, gelled by crosslinking) with calcium ions (col. 3, lines 54-61). Even though Agerup use alginate as a carrier, one of skill in the art will recognize, based on the teaching of Marler that alginate itself could be used for augmentation either alone or in combination with other agents.

Vanderhoff et al teach polymer particles of about 150 micrometers for use in soft tissue augmentation (page 4, line 20 through page 5, line 4). The injectable particles can also contain encapsulated drugs and medications (page 5, lines 5-9; lines 25-31; page 7, lines 6-35). The water soluble polymers can be polysaccharides (page 8, lines 32-34). One of the desirable polymers is sodium alginate, since it is biocompatible, biodegradable, and non immunogenic and in the form of microspheres is a good candidate as carrier of drugs (page 9, lines 7-20). Several types of crosslinking agents can also be used depending upon the polymer used and can be readily determined by one of skill in the art (page 9, lines 21-35). For crosslinking of the microparticles, pH can be adjusted to adjust the rate of crosslinking (page 10, lines 20-21). Even though Vanderhoff's teaching is drawn to a process for producing microparticles, he suggests the use of such particles for tissue augmentation. One of skill in the art will use such microparticles of alginate for tissue augmentation as taught by Marler, Bent and Agerup.

The Merck Index and Hawley's both teach that gluconolactone and EDTA are complexing (sequestering) agents.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use alginates, crosslinked and uncrosslinked, in the form of microspheres, for increasing the volume of tissue in a subject, as instantly claimed since the use of such is taught using analogous alginates for the same purpose.

One of skill in the art would be motivated to use alginates in the method as instantly claimed since Marler teaches that the use of alginates offers additional advantages like chemical modification to induce desirable properties, is readily available and has been approved by FDA for use in human patients (Marler, page 2054, right column, first and second paragraphs). According to Vanderhoff, one of the desirable polymers is sodium alginate, since it is biocompatible, biodegradable, and non immunogenic and in the form of microspheres is a good candidate as carrier of drugs (page 9, lines 7-20). With so many advantages, one of skill in the art would prefer to use alginate over other polymers suggest in the prior art.

One of skill in the art would also prefer to use EDTA or gluconolactone since both are taught to be sequestering agents. Their ability to form covalent bonds would be an advantage in addition to ionic bonds formed by the metal ions during crosslinking (Vanderhoff page 9, line 35 through page 10 line 1). The use of citrate is also logical since it is a component of the well know citrate buffer used for adjusting pH. In line with the teaching of Vanderhoff regarding the adjustment of pH for adjusting the rate of crosslinking use of the biocompatible citrate is preferable (Vanderhoff page 10, lines 20-21). It is well within the skill level of the artisan to adjust the percentages of the agents and the size of the microparticle as a routine optimization based on the ranges taught in the prior art.

Conclusion

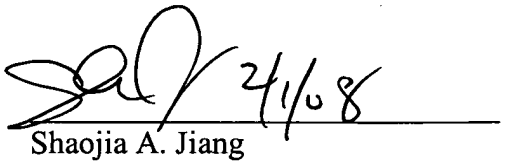
Claims 22-48 are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GK



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